PEC UPDATE

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ISSUE HIGHLIGHTS

Happy Holidays from the PEC Staff!

In the Literature.....

Interim Results of AHCPR-Sponsored Study on Stroke Prevention

The Agency for Health Care Policy and Research (AHCPR) has recently announced preliminary results of a Patient Outcomes Research Team (PORT) study on stroke prevention in patients at high risk. The study found that warfarin is not being used appropriately to prevent stokes.[1,2]

About 5% of all people over the age of 60 have atrial fibrillation which increases their risk for stroke. However, in spite of clinical trials showing warfarin as the optimal treatment for the majority of patients 60 years of age and older who have atrial fibrillation, it is only used in about one-quarter of these patients, and only half of these patients receive the optimal dosage. The PORT researchers estimate that 50 to 75% of patients over 60 years of age with atrial fibrillation should be receiving warfarin therapy. If warfarin were used appropriately, researchers estimate it could cut the stroke rate in half and save approximately $600 million annually in medical costs.[1,2] Anticoagulation therapy is not necessary for most atrial fibrillation patients under age 60 because they have a much lower risk of stroke.[1,3]

Many physicians underutilize warfarin because of the difficulties in monitoring patients and the concerns about bleeding. Warfarin does increase the risk of bleeding, but for every bleeding complication that occurs with warfarin, 20 strokes are prevented. Although regular monitoring of warfarin therapy is necessary, it can be provided on an outpatient basis by pharmacists or nurse practitioners with little physician involvement.[1,2] Anticoagulation monitoring clinics provide an excellent opportunity for pharmacists to provide pharmaceutical care.

Guidelines for medical treatment for stroke prevention were published in July 1994 by the American College of Physicians

(ACP).[3] The American College of Chest Physicians made the same recommendations in 1992.[4] The ACP recommendations are listed below for your information. Use of these recommendations is ultimately based on a clinical judgment of the benefit versus risk.

- **Nonvalvular atrial fibrillation:** Warfarin is the drug of choice for patients who are candidates for anticoagulation. Patients younger than 60 years of age with no risk factors do not need warfarin therapy. Patients on warfarin therapy require careful monitoring of the intensity of anticoagulation based on the international normalized ratio (INR), with the ideal ratio between 2 and 3. Aspirin 325 mg daily is an appropriate alternative for patients unwilling or unable to take warfarin. Aspirin may not be effective in patients older than 75 years of age.
- **Transient ischemic attack (TIA) and stroke:** Aspirin is effective in reducing the stroke risk in patients with TIA and minor stroke, but the benefit-to-risk ratio is about 5:2. All aspirin doses studied are similarly effective, so the dose should be based on patient tolerance. No evidence suggests that aspirin reduces the risk for stroke in patients who have had a major stroke, but it is a reasonable option. Patients who cannot tolerate or do not respond to aspirin may be given ticlopidine, but they must be supervised on the drug.
- **Previous myocardial infarction (MI):** Warfarin appears to reduce the risk of stroke in patients who have had MI, but the benefit-to-risk ratio is 3:2 because of bleeding complications. These complications may be caused by the use of high-intensity anticoagulation (INR, 2.5 to 4.8). Lower levels of anticoagulation are safer, making warfarin a clear recommendation, if these levels are as effective. Aspirin is an alternative treatment for stroke reduction in patients who have had MI, but the benefits appear to be small. For patients who have had MI, neither anticoagulation nor antiplatelet drugs are specifically recommended for stroke reduction; however, these agents may help reduce the incidence of all nonfatal vascular events.

References:
1. Anonymous. Life-saving treatment to prevent stroke underused. *Research Activities* 1995 September;187:1-3.
2. Anonymous. Used correctly, the anticoagulant warfarin could cut stroke risk in half. *Drug Utilization Review* 1995;11(11):161-3.
3. American College of Physicians. Guidelines for medical treatment for stroke prevention. *Ann Intern Med* 1994;121:54-5.
4. Laupacis A, Albers G, Dunn M, Feinberg W. Antithrombotic therapy in atrial fibrillation. *Chest* 1992;102(Suppl):426S-433S.

Beta-Blockers, Diuretics, and Calcium-Channel Blockers:
Articles Contributing to the Controversy

Several articles in the literature have contributed to the controversy over the use of beta-blockers, diuretics, and calcium-channel blockers in various cardiovascular conditions. These references are listed below for your information.

- Kendall MJ, Lynch KP, Hjalmarson A, Kjekshus J. ß-Blockers and sudden cardiac death. *Ann Intern Med* 1995;123:358-67.
- Hoes AW, Grobbee DE, Lubsen J, Man in 't Veld AJ, van der Does E, Hofman A. Diuretics, ß-blockers, and the risk for sudden cardiac death in hypertensive patients. *Ann Intern Med* 1995; 123:481-7.
- Psaty BM, Heckbert SR, Koepsell TD, et al. The risk of myocardial infarction associated with antihypertensive drug therapies. *JAMA* 1995; 274:620-5.
- Buring JE, Glynn RJ, Hennekens CH. Calcium channel blockers and myocardial infarction: a hypothesis formulated but not yet tested [editorial]. *JAMA* 1995;274:654-5.
- Furberg CD, Psaty BM, Meyer JV. Nifedipine: dose-related increase in mortality in patients with coronary heart disease. *Circulation* 1995; 92: 1326-31.
- Opie LH, Messerli FH. Nifedipine and mortality: grave defects in the dossier [editorial]. *Circulation* 1995; 92:1068-73.
- Kloner RA. Nifedipine in ischemic heart disease [editorial]. *Circulation* 1995;92:1074-78.

- Yusuf S. Calcium antagonists in coronary artery disease and hypertension: time for reevaluation? [editorial]. *Circulation* 1995;92:1079-82.
- Lenfant C. The calcium channel blocker scare. Lessons for the future. *Circulation* 1995;91: 2855-6.
- Fagan TC. Calcium antagonists and mortality: another case of the need for clinical judgment [editorial]. *Arch Intern Med* 1995;155:2145.
- Epstein M. Calcium antagonists should continue to be used for first-line treatment of hypertension [commentary]. *Arch Intern Med* 1995;155:2150-6.
- Furberg CD, Psaty BM. Should dihydropyridines be used as first-line drugs in the treatment of hypertension? The con side [commentary]. *Arch Intern Med* 1995;155:2157-61.

From the Mailbag.....

PEC Q & A

Q: I have some patients who have been receiving omeprazole for longer than 8 weeks of therapy for gastroesophageal reflux disease (GERD). What is the PEC recommendation for the use of omeprazole in GERD?

A: Omeprazole 20-40 mg QD for 4-8 weeks is the recommended treatment for the initial episode of severe GERD in the PEC guideline on acid-peptic diseases (PEC Update 94-09). If a patient responds to a course of omeprazole therapy, maintenance therapy may not be necessary at this point, and the patient should be retreated as symptoms recur. However, relapse rates of severe esophagitis can be as high as 80 to 90% in 1 year without maintenance therapy. If the patient has little or no response to initial therapy, or has a relapse, he/she should be evaluated by a gastroenterologist and may require long-term maintenance therapy or other interventions. The PEC guideline does not provide recommendations for treatment of refractory patients since subspecialty management is indicated for these patients.

Probucol Withdrawn from Market

Hoechst Marion Roussel notified the FDA on October 10, 1995 of the withdrawal of the cholesterol-lowering agent probucol (Lorelco®) from the market. Probucol lowers LDL cholesterol levels; however, it also lowers HDL cholesterol levels, an unfavorable lipid effect. The FDA began considering the withdrawal of the drug about a year ago because of concerns over probucol's efficacy and not because of any specific adverse event reports. Probucol has been reported to cause prolongation of the QT interval and serious arrhythmias in patients receiving the drug alone or concomitantly with antiarrhythmic agents.

Probucol was not included in the pharmacoeconomic analysis of hyperlipidemia because its role in the treatment of elevated cholesterol levels is not clear, particularly given its effects on HDL cholesterol.

From: *FDC Reports* 1995; 57(42):T&G 1.

New Price Contracts and Pharmaceutical Price Reductions

Lemmon Pharmaceuticals

Lemmon Pharmaceuticals was selected for the VA National Contract for gemfibrozil 600 mg tablets. The assigned contract number is 797EA500665, effective September 12, 1995:

NDC	*Product/Package*	*FSS Price*
0093-0670-06	Gemfibrozil 600 mg, 60s	$6.00
0093-0670-05	Gemfibrozil 600 mg, 500s	$50.00

If you experience problems obtaining Lemmon's

gemfibrozil through your prime vendor wholesaler or require additional information, please contact Lemmon's Customer Service Department at (800) 545-8800.

Creighton Products/Sandoz Pharmaceuticals

Effective October 15 through December 31, 1995, Creighton Products Corporation, a subsidiary of Sandoz Pharmaceuticals Corporation, is offering the following price reductions on nortriptyline hydrochloride capsules available on Federal Supply Schedule - Section B, Contract No. V797P-5725N.

NDC	*Product/Package Size*	*FSS Price*
50752-251-05	Nortriptyline 25 mg, 100s	$7.52
50752-251-08	Nortriptyline 25 mg, 500s	$34.50
50752-252-05	Nortriptyline 50 mg, 100s	$8.85
50752-253-05	Nortriptyline 75 mg, 100s	$11.18

Penn Labs/SmithKline Beecham Pharmaceuticals

Penn Labs Inc., a wholly owned subsidiary of SmithKline Beecham Pharmaceuticals, has announced the following price reductions on cimetidine tablets, Federal Supply Schedule Contract No. V797P-5587m, effective through December 31, 1995.

NDC	*Product/Package Size*	*FSS Price*
58437-001-20	Cimetidine 300 mg, 100s	$11.98
58437-001-25	Cimetidine 300 mg, 500s	$57.05
58437-002-18	Cimetidine 400 mg, 60s	$11.13
58437-002-25	Cimetidine 400 mg, 500s	$90.25
58437-003-13	Cimetidine 800 mg, 30s	$10.08

Purchasers should remember that transaction costs are incurred when products are ordered by local purchase versus prime vendor. These costs may negate potential savings from slightly lower priced products not available through the prime vendor.

Association for Pharmacoeconomics and Outcomes Research

The Association for Pharmacoeconomics and Outcomes Research (APOR) is a new organization dedicated to promoting and advancing the science of pharmacoeconomics. Unlike other pharmacy organizations, APOR is dedicated solely to the field of pharmacoeconomics. It began operations this summer and already includes over 300 members representing a diverse group of individuals from academia, industry, and government. The PEC had the privilege of being invited to contribute to the founding of this organization, especially in the area of applied pharmacoeconomics.

Anyone seriously interested in the field of pharmacoeconomics should consider joining this organization. Membership in the organization is $75 per year. The first annual meeting is planned for May 12-15, 1996 in Philadelphia, and a full schedule of interesting and informative topics has been established. Abstracts for poster sessions are being accepted through the month of December, if you have any interesting studies you would like to present.

Questions concerning APOR can be directed to LTC Steven Finder at the PEC. Inquires can also be addressed to APOR directly at the following address and telephone number:

APOR, Suite 319, CN 5256, Princeton, NJ 08543-5256
(609) 497-2203
EMail: Econhealth@aol.com

1996 Ambulatory Care Pharmacist Pharmacoeconomics Conference

Mark your calendars now—the 1996 Ambulatory Care Pharmacist/Pharmacoeconomics Conference is almost here. The conference will be held at the Hilton Palacio del Rio on the Riverwalk in San Antonio, Texas on January 8-12, 1996. A poster session has been organized to give participants the opportunity to highlight the pharmacy activities at their facility. All attendees are encouraged to present a poster.

Anyone interested in attending the conference or presenting a poster should contact Jill Williams at The University of Texas at Austin, College of Pharmacy at (512) 471-6213.